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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,687	01/09/2001	Patrick Mark Curry	273012011120	4676

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MORRISON & FOERSTER LLP
3811 VALLEY CENTRE DRIVE
SUITE 500
SAN DIEGO, CA 92130-2332

EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/756,687	CURRY ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *December 8, 2003 and January 14, 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 28-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21 and 28-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed on December 8, 2003 and the supplemental amendment filed January 14, 2004 are acknowledged and have been entered. Claims 1-3 have been amended.

2. Claims 1-21 and 28-33 are pending in the application and are currently under continued prosecution.

Grounds of Objection and Rejection Withdrawn

3. Unless specifically reiterated below, the grounds of objection and rejection set forth in the previous Office action mailed June 6, 2003 have been withdrawn.

Priority

4. Applicant's claim for priority under 35 USC § 120 of the earlier filing date of prior US Application No. 09/556,833 filed September 22, 2000, which claims the benefit of the earlier filing date of US Provisional Application No. 60/130,519 filed April 23, 1999 is acknowledged. However, the prior provisional application fails to provide adequate support under 35 U.S.C. 112 for claims 1-21 and 28-33 of this application. In particular, the prior provisional application does not disclose the combination of GM-CSF or Flt-3 ligand together with a green porphyrin photosenstizer and an immunoadjuvant. To receive benefit of the earlier filing date under 35 USC § 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). Accordingly, the effective filing date of this application

is considered to be the date US Application 09/556,833 was filed, namely April 21, 2000.

Response to Amendment

5. Applicant's arguments with respect to the rejections of the claims under 35 USC § 103(a) for the reasons set forth in section 8 of the previous Office action mailed June 6, 2003 have been considered but are moot in view of the new grounds of rejection under 35 USC § 103(a).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-3, 5-7, 9-11, 13, 14, 16, 21, 28, and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) and Krosl et al. (Cancer Research 56: 3281-3286, 1996), as evidenced by Kresl et al. (*Tumour Biol.* **20**: 72-87, 1999).

Claims 1-3, 5-7, 9-11, 13, 14, 16, 21, 28, and 30-32 are drawn to a method for treating primary or metastatic tumors, or for preventing or inhibiting the development of the latter in a subject by photodynamic therapy and immunotherapy comprising administering to the subject one or more green porphyrin photosensitizers, one or more immunoadjuvants, and GM-CSF and irradiating the subject.

Korbelik et al. teaches a method for treating tumors in a subject comprising administering to the subject effective amounts of a green porphyrin, namely benoporphyrin derivative monoacid (BPD-MA), Photofrin™, or mTHPC chlorin, and an immunoadjuvant, namely a mycobacterial cell wall extract or live Bacillus Calmette-

Guerin (BCG) vaccine and irradiating the subject with light comprising a wavelength absorbed by said photosensitizer; see, e.g., "Abstract" at page 151; "Materials and Methods" at page 152; and "Results" at page 154. Korbelik et al. teaches administering the immunoadjuvant as an adjuvant to photodynamic therapy (PDT) enhances the antitumor effects of PDT; see, e.g., "Abstract" and "Discussion". Korbelik et al. teaches a curative effect of the treatment, since the treated mice remain tumor-free; see, e.g., "Fig. 1" at page 153. Depending upon the photosensitizer, Korbelik et al. teach an effective amount of the photosensitizer is in the range of 0.05 to 10, 0.05 to 1, or 1 to 10 milligrams of photosensitizer per kilogram of subject; see, e.g., "Fig. 2" at page 154; and "Fig. 3" at page 154. Korbelik et al. teaches irradiation is localized to the tumor; see "Materials and Methods" at page 152, column 1. Korbelik et al. teaches the photosensitizer is administered intravenously (*or systemically*); see "Fig. 2" at page 154. Korbelik et al. teaches the photosensitizer can be administered to the subject, and the subject can be irradiated - before the immunoadjuvant is administered to the subject; see "Results" at page 154.

Korbelik et al. teaches the preparation of mycobacterial cell wall extract, which is used is purified and deproteinized, and sold under the tradename Regressin by Bioniche Inc. (London); see "Materials and Methods" at page 152, column 1. Therefore, absent a showing any difference, the bacterial cell wall extract of Korbelik et al. is deemed the same as or otherwise deemed to comprise, the immunoadjuvant of the claims, which is "mycobacterial cell wall skeletons".

As evidenced by Kresl et al., mice implanted subcutaneously with mouse mammary adenocarcinoma line EMT6 cells are at risk for developing tumors from metastasis of the primary tumor. Since Korbelik et al. teaches a curative effect by the treatment, since the treated mice remain tumor-free, it appears the method of Korbelik et al. can be used to prevent or inhibit in a subject at risk for developing tumors from metastasis of a primary tumor the development of such tumors.

Krosl et al. discloses GM-CSF is a key regulator controlling the maturation and function of granulocytes and monocytes/macrophages and the activation of these cells had previously been shown to potentiate the curative effect of PDT (page 3281, column

2). Krosl et al. discloses, to investigate the effect of localized GM-CSF treatment on the control of tumors treated with photodynamic therapy (PDT), the gene encoding GM-CSF was introduced into tumor cells, which were lethally irradiated and injected intratumorally into mice before initiating PDT; see, e.g., "Materials and Methods" at pages 3282 and 3283; and "Discussion" at page 3285, column 1. Krosl et al. teaches GM-CSF immunotherapy administered three times at two day intervals, starting two days before the light treatment, substantially improves the curative effect of Photofrin™-mediated PDT; see, e.g., the abstract. Krosl et al. discloses the rationale for combining a cytokine, such as GM-CSF, which is capable of stimulating a potent systemically acting T-cell-mediated antitumor immune response (page 3281, columns 1 and 2). Krosl et al. discloses that in their instant study, it was determined that, whereas tumors recurred in mice treated with PDT alone, the combination of GM-CSF immunotherapy and PCT prolonged the tumor free period and led to an overall cure rate of 75% (page 3284, column 2). Krosl et al. disclose that similar results were achieved using benzoporphyrin monoacid (BPD-MA) (page 3284, column 2). Krosl et al. discloses the response to PDT of tumors characterized by different degrees of immunogenicity has been shown by nonspecific immune stimulants, including glucan Schizophyllen, Bacillus Camette Guerin (BCG), *Corynebacterium parvum* vaccine, mycobacterial cell wall extract (MCWE), endotoxin, as well as specific immune agents such as the macrophage-activating factor GcMAF and cytokines TNF-α and IL-7 (page 3285, column 2). Krosl et al. further discloses that their results are particularly encouraging with respect to potential clinical ramifications, since potentiation of the antitumor immune response by PDT has been demonstrated using a tumor that is poorly immunogenic (page 3285, column 2). Finally, Krosl et al. concludes, "due to its unique inflammatory/immune character, PDT is highly responsive to adjuvant immunotherapy" (page 3285, column 2).

While Korbelik et al. teaches administering the mycobacterial cell wall extract (MCWE) or Bacillus Camette Guerin (BCG) as an adjuvant to photodynamic therapy (PDT) enhances the antitumor effects of PDT, Krosl et al. teaches administering GM-CSF as an adjuvant to PDT potentiates the curative effects of PDT; therefore, it would

have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to combine the treatments of Korbelik et al. and Krosl et al. to treat a subject clinically diagnosed as having a primary or metastatic tumor, or a subject at risk for developing metastatic tumors. In addition, it is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; the idea of combining them flows logically from their having been individually taught in prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980. See MPEP § 2144.06. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat cancer in a subject.

8. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) and Krosl et al. (Cancer Research 56: 3281-3286, 1996), as applied to the rejection of claims 1-3, 5-7, 9-11, 13, 14, 16, 21, 28, and 30-32 above, and in further view of Momma et al. (*Cancer Research* **58**: 5425-5431, 1998).

Claim 4 is drawn to the method of claim 2, wherein the subject has previously undergone cancer or tumor therapy.

Korbelik et al. and Krosl et al. teach that which is set forth above.

However, neither Korbelik et al. nor Krosl et al. expressly disclose treating a subject that has previously undergone anticancer therapy.

Momma et al. teaches a BPD-MA can be used to effectively treat, inhibit, or prevent primary and secondary tumors by photodynamic therapy; see, e.g., "Abstract". Momma et al. teaches the treatment can be used as an adjuvant to surgical treatment, so Momma et al. teaches the subject has previously undergone anticancer therapy.

Because Momma et al. teaches photodynamic therapy can be used to effectively treat, inhibit, or prevent primary and secondary tumors after surgery, while Korbelik et al. and Korsl et al. teach administering MCWE and GM-CSF, respectively, as adjuvants to photodynamic therapy (PDT) enhances the antitumor effects of PDT, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to further treat a subject at risk for developing a secondary tumor, or *metastasis* using the

combination treatment of Korbelik et al. and Krosl et al. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat cancer in a subject.

9. Claims 8, 12, 18, 19, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) and Krosl et al. (Cancer Research 56: 3281-3286, 1996), as applied to the rejection of claims 1-3, 5-7, 9-11, 13, 14, 16, 21, 28, and 30-32 above, and in further view of US Patent No. 5,579,554 A.

Claim 8 is drawn to the method of claim 1, wherein the photosensitizer is administered intraveneously and the immunoadjuvant is administered by injection into tumors after irradiation, whereas claims 18 and 19 are drawn to the method of claim 8, wherein the immunoadjuvant is additionally administered systemically at least 1-3 times at intervals of about 2 weeks. Claim 12 is drawn to the method of claim 1, wherein the immunoadjuvant is administered systemically. Claim 29 is drawn to the method of claim 2, wherein the photosensitizer is administered intraveneously and the immunoadjuvant is administered by injection into tumors after irradiation.

Korbelik et al. and Krosl et al. teach that which is set forth above.

However, while Korbelik et al. and Krosl et al. teach the immunoadjuvant is administered subcutaneously under the tumor, or *peritumorally* after irradiation, neither reference expressly teaches or suggests that the immunoadjuvant can be administered intratumorally (claim 8) or systemically (claim 12).

US Patent No. 5,759,554 A ('554) teaches an aqueous mycobacterial cell wall extract, which can be injected directly into the tumor or it can be given systemically (column 5, lines 14-24). '554 teaches administering to a subject the disclosed aqueous mycobacterial cell wall extract is an effective means for treating cancer; see, e.g., abstract. '554 discloses: "The cancers can be primary or metastatic" (column 3, lines 42-45). The advantage that the immunoadjuvant of '554 provides is that it does not need to be suspended in oil and therefore its use precludes the development of granulomas in subjects treated with immunoadjuvants comprising oil (column 4, lines 5-

9; column 2, lines 39-42). '554 teaches the immunoadjuvant can be administered repeatedly up to five times at intervals of at least one week without frequently causing hypersensitivity to diminish the number of metastases to the lung and lymph nodes; see, e.g., column 4, line 66, through column 5, line 4.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to administer the immunoadjuvant intratumorally or systemically in practicing the combined method of Korbelik et al. and Krosl et al., because '554 teaches the immunoadjuvant can be administered intratumorally or systemically. Because '554 teaches administering to a subject the disclosed aqueous mycobacterial cell wall extract is an effective anticancer treatment, while Korbelik et al. teaches administering an immunoadjuvant, such as the immunoadjuvant of '554 as an adjuvant to photodynamic therapy (PDT) enhances the antitumor effects of PDT, the artisan would have had a reasonable expectation of success in doing so at the time of the invention. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat cancer in a subject.

10. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) and Krosl et al. (Cancer Research 56: 3281-3286, 1996), as applied to the rejection of claims 1-3, 5-7, 9-11, 13, 14, 16, 21, 28, and 30-32 above, and in further view of US Patent No. 6,071,944 A.

Claim 15 is drawn to the method of claim 1, which comprises an additional step comprising additional irradiation, before irradiation with light of a wavelength absorbed by the photosensitizer, with a light of a wavelength that improves penetration of the wavelength of light absorbed by the photosensitizer.

Korbelik et al. and Krosl et al. teach that which is set forth above.

However, neither Korbelik et al. nor Krosl et al. expressly teaches or suggests the inclusion of an additional step comprising additional irradiation, before irradiation with light of a wavelength absorbed by the photosensitizer, with a light of a wavelength that increases penetration of the wavelength of light absorbed by the photosensitizer (claim 15).

US Patent No. 6,071,944 A ('944) teaches a method for treatment of malignant melanoma, which also comprises administering to the subject a photosensitizer and then irradiating the subject at a wavelength at which the photosensitizer absorbs light; see, e.g., abstract. '944 discloses that the efficacy of photodynamic therapy can be hampered if lesions are pigmented, which is often the case with highly metastatic melanoma, because the pigmented tumor cells are less responsive; the lack of response attributed to optic filtering by melanin granules within the cell; see, e.g., column 1, lines 29-38. As a solution to the problem, '944 teaches that pretreatment of pigmented tumors with high peak power light (such as 1064 nm light) enhances their susceptibility to conventional photodynamic therapy; see, e.g., column 3, lines 35-46. Therefore, '944 teaches that photodynamic therapy is more efficacious when the subject is irradiated at a wavelength that improves penetration of the wavelength of light at which the photosensitizer absorbs.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to add a step to the combined method of Korbelik et al. and Krosl et al., which step comprises an additional irradiation with light of a wavelength that improves penetration of the absorbed light before irradiating the subject at the wavelength absorbed by the photosensitizer, because '944 teaches that photodynamic therapy is more efficacious when the subject is first irradiated at a wavelength that improves penetration of the wavelength of light at which the photosensitizer absorbs, especially if the tumor cells are pigmented. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat cancer in a subject.

11. Claims 17 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) and Krosl et al. (Cancer Research 56: 3281-3286, 1996), as applied to the rejection of claims 1-3, 5-7, 9-11, 13, 14, 16, 21, 28, and 30-32 above, and in further view of Johnston et al. (*J. Natl. Cancer Inst.* **83**: 1240-1245, 1991) and US Patent No. 4,912,094 A.

Claim 17 and 33 are drawn to the method of claims 1 or 2, respectively, wherein one or more immunoadjuvant comprises mycobacterial cell wall skeleton and lipid A from a gram negative bacterium, wherein said lipid A is de-3-O-acylated lipid A.

Korbelik et al. and Krosl et al. teach that which is set forth above.

However, while Korbelik et al. teaches or suggests the immunoadjuvant is a mycobacterial cell wall extract comprising mycobacterial cell wall skeletons, neither reference not expressly teaches or suggests an immunoadjuvant comprising mycobacterial cell wall skeleton *and de-3-acylated lipid A*.

Johnston et al. teaches an immunoadjuvant comprising purified mycobacterial cell wall skeleton and monophosphoryl lipid A (MPL). Johnston et al. teaches the immunoadjuvant can be administered more safely than Freund's complete adjuvant, since the immunoadjuvant induced fewer cutaneous toxic effects, but produced stronger antibody and delayed-type hypersensitivity responses than Freund's complete adjuvant; see, e.g., the abstract. Johnston et al. discloses the combination of mycobacterial cell wall skeleton and monophosphoryl lipid A (MPL), as in DETOX, has been reported to have a synergistic effect (page 1243, column 2).

US Patent No. 4,912,094-A ('094) teaches that modified lipopolysaccharides, particularly de-3-O-acylated monophosphoryl lipid A and de-3-O-acylated diphosphoryl lipid A retain a high level of immunostimulating capacity but have the advantage of being considerably less endotoxic than naturally occurring lipopolysaccharide (abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the combined method of Korbelik et al. and Krosl et al. using an immunoadjuvant comprising mycobacterial cell wall skeleton and de-3-acylated lipid A because Johnston et al. teach the combination of mycobacterial cell wall skeleton and MPL produces a synergistic effect, and because '094 teaches de-3-acylated lipid A is considerably less endotoxic than naturally occurring lipopolysaccharide. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat cancer in a subject.

12. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) and Krosl et al. (Cancer Research 56: 3281-3286, 1996), as applied to the rejection of claims 1-3, 5-7, 9-11, 13, 14, 16, 21, 28, and 30-32 above, and in further view of US Patent Nos. 5,756,541-A and 5,579,554 A.

Claim 20 is drawn to the method of claim 1, wherein the steps of administering and irradiating are repeated at least 1-3 times.

Korbelik et al., Krosl et al., and US Patent No. 5,579,554 A ('544)teach that which is set forth above. In addition, Krosl et al. teaches GM-CSF is administered to the subject more than once (page 3282, column 2).

However, neither reference expressly teaches or suggests that the treatment regimen can be repeated 1-3 times.

US Patent No. 5,756,541-A ('541) teaches that a regimen of photodynamic therapy using "green porphyrins" or benzoporphyrin derivatives, such as BPD-MA, can be repeated two times to provide an improvement in the result of the therapy (column 7, lines 5-21).

Krosl et al. teaches GM-CSF is administered to the subject more than once, '554 teaches the immunoadjuvant is administered more than once, and '541 teaches repeating photodynamic treatment provides improved therapeutic results; therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to repeat the combination treatment of Korbelik et al. and Krosl et al. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat cancer in a subject.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR § 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR § 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR § 3.73(b).

14. Claims 1-17 and 28-33 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 09/556,833 for the reasons set forth in the section 10 of the previous Office action mailed June 6, 2003.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

At Applicant's request, this issue will be held in abeyance until such time that patentable subject matter is indicated; see page 17 of the amendment filed December 8, 2003.

Conclusion

15. No claims are allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. The prior art made of record, but not relied upon is considered pertinent to Applicants' disclosure. Chen et al. teaches antitumor and immunotherapeutic properties of Flt3-ligand. Chakravarty et al. teaches Flt3-ligand administration after radiotherapy prolongs survival. Lynch et al. (1997) teaches Flt3-ligand induces tumor regression and antitumor immune responses. Lynch et al. (1998) teaches induction of dendritic cells by Flt3-ligand promotes the generation of tumor-specific immune responses. Ciavarra et al. teaches Flt3-ligand induces tumor regression. Korbelik et al. (*J. Clin. Laser Med. Surg.* **14**: 329-334, 1996; cited by Applicant) reviews induction of tumor immunity by photodynamic therapy (PDT). Korbelik et al. (*Photochem. Photobiol.* **60**: 497-502, 1994) teaches enhanced macrophage cytotoxicity against tumor cells treated with PDT. Krosl et al. (*Cancer Lett.* **60**: 43-49, 1994; cited by Applicant) teaches potentiation of PDT by immunotherapy.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
April 20, 2004

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600